41 have been withdrawn from further consideration. No new matter is added by this Amendment.

ELECTIONS/RESTRICTIONS:

Applicants affirm their September 3, 2002 election of the Group I claims.

INFORMATION DISCLOSURE STATEMENT:

Applicants request clarification of Paragraph 3 of the Office Action, which states that the IDS filed on July 30, 2002 "fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent." The last sentence of Paragraph 3 states that the IDS "has been placed in the application file, but the information referred to therein has not been considered."

For three reasons, Applicants believe that Paragraph 3 or at least its last sentence was included in error. First, Applicants' records indicate that copies of the references were submitted with the IDS, and Applicants' undersigned counsel recalls submitting them. Second, the Examiner initialed all of the references on the IDS form. Third, the main reference applied as prior art in the Office Action is one of the references submitted with the IDS.

On November 13, 2002, Applicants telephoned the Examiner about Paragraph 3. The Examiner appeared to agree that Paragraph 3 may have been included in error but could not confirm it because he did not have the file at the time. Before the Examiner could obtain and review the file, he was forced to take leave due to a family emergency. On December 20, 2002, Applicants spoke by telephone with Supervisor Gary Benzion about Paragraph 3. He suggested that Applicants request clarification in their response. He also reminded Applicants that, if the Examiner initialed the IDS, the PTO presumes that the Examiner reviewed the references.

OBJECTIONS TO DRAWINGS:

In Paragraph 4 of the Office Action, the Examiner objected to the lack of description of Figures 1-6 in the specification. The specification has been amended to include a Brief Description of the Figures, which recites the descriptions that appear explicitly or implicitly in Figures 1-6.

OBJECTIONS TO SPECIFICATION:

In Paragraph 5, the Examiner objected to the title that appeared above the Abstract. The Abstract is now entitled Abstract of the Disclosure.

With regard to Paragraph 6, Applicants thank the Examiner for suggesting a layout. However, Applicants prefer to retain the current layout for the most part.

OBJECTIONS TO CLAIMS:

The amendments to claims 1-36 cure the objections of Paragraphs 7, 8 and 9 of the Office Action.

REJECTIONS OF CLAIMS FOR INDEFINITENESS:

The amendments to claims 1-36 cure the rejections of Paragraph 10 of the Office Action.

Please note that the amendments change the letter designation for some of the steps. In the original claims, steps were first designated by letters in claim 2, as steps (a), (b), (c) and (d). Originally, step (a) designated the step of "fragmentation of a bank," step (b) designated "denaturation of fragments," step (c) designated "hybridization of fragments," and step (d) designated "oriented ligation of said fragments." Original claim 3 designated step (e) "the selection of recombinant polynucleotide sequences."

Now, designations start in claim 1, wherein step (a) designates "providing oligonucleotide fragments," step (b) designates "hybridizing the fragments," and step (c) designates "ligating the oriented fragments." In claim 3, step (d) designates "selecting recombinant polynucleotide sequences." The phrase "denaturing the fragments" now appears in claim 4 as a substep of step (a).

REJECTIONS OF CLAIMS FOR ANTICIPATION:

In Paragraph 11 of the Office Action, the Examiner rejected claims 1-3, 11-18, 20, 24-28 and 31-36 under 35 USC 102(e) in view of Stemmer et al (US2001/0049104A1), which was filed on March 23, 2001, and which claims the benefit of provisional applications filed on January 17, 2001 and March 24, 2000.

Applicants respectfully disagree with the Examiner's characterization of what Stemmer et al discloses. However, argument is unnecessary because Stemmer et al cannot qualify as prior art under 102(e) in view of Applicants' earlier effective filing date. As discussed in Applicants' Petition to accept a late claim for priority, filed herewith, the above-captioned application is a CIP of a U.S. application filed on November 28, 2000, which is entitled to the benefit of a PCT application filed on August 11, 1999 and a French application filed on August 12, 1998.

REJECTIONS OF CLAIMS FOR OBVIOUSNESS:

In Paragraph 13, the Examiner rejected claim 19 as obvious over Stemmer et al in view of Prudent et al. In Paragraph 14, he rejected claims 21 and 23 as obvious over Stemmer et al in view of Auerbach et al. Since the main reference, Stemmer et al, is unavailable as prior art, these rejections must also fail.

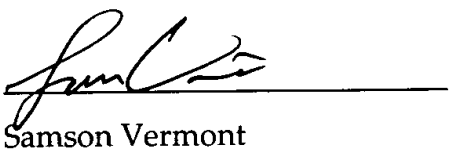
In light of the foregoing, Applicants respectfully request withdrawal of all outstanding objections and rejections. The Examiner is welcome to contact undersigned counsel if the Examiner has any questions or comments.

Filed herewith is a check to cover the claims added by this Amendment. Applicants believe that no additional fees are due. However, in the event that any fees are due, the Director is hereby authorized to charge our Deposit Account No. 50-0206.

Respectfully submitted,

HUNTON & WILLIAMS

Dated: December 24, 2002

By: 

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Appendix A

Marked-Up Version of Amended Claims

1. A method [Process] of creating at least one recombinant polynucleotide sequence [characterized in that it comprises a step of oriented ligation of] , comprising:

(a) providing oligonucleotide fragments derived from [a] an initial bank of at least two polynucleotide sequences ;

(b) hybridizing the fragments to an assembly matrix so that the fragments are oriented for ligation with each other; and

(c) ligating the oriented fragments to form a recombinant polynucleotide sequence.

2. [Process according to] The method of claim 1, wherein step (a) comprises fragmenting polynucleotide sequences from the [it comprises the following steps: a) fragmentation of a] bank of polynucleotide sequences [, b) denaturation of the fragments thus obtained, c) hybridization of fragments obtained in step (b) with one or several assembly matrix (matrices), d) oriented ligation of said fragments to obtain at least one recombinant polynucleotide sequence] .

3. [Process according to claim 2, wherein it comprises after step (d): e) the selection of]

The method of claim 1, further comprising step (d) selecting recombinant polynucleotide sequences formed at step (c) that exhibit [offering] advantageous

characteristics compared to corresponding characteristics of one or several reference sequences.

4. [Process according to claims 1 to 3] The method of claim 3, wherein the bank of polynucleotide sequences contains double-stranded polynucleotide sequences and step (a) further comprises denaturing the fragments obtained at step (a).

5. [Process according to claims 1 to 3] The method of claim 1, wherein the bank of polynucleotide sequences contains single-stranded polynucleotide sequences.

6. [Process according to claims 2 to 5] The method of claim 1, wherein at least one assembly matrix is double-stranded and it is first denatured [to be] and then added in single-stranded form at step (b) [(c)] .

7. [Process according to claims 2 to 5] The method of claim 1, wherein at least one assembly matrix is single-stranded.

8. [Process according to claims 2 to 7, wherein it comprises,] The method of claim 1, further comprising at the end of step (c) [(d),] at least one repetition of steps (a), (b), or (c) [(c), and (d)].

9. [Process according to claims 2 to 7, wherein it comprises,] The method of claim 1, further comprising at the end of step (c) [(d),] at least one repetition of steps (b) or (c) [, (c), and (d)].

10. [Process according to claims 3 to 7, where it comprises,] The method of claim 3, further comprising at the end of step (d), [(e)] a step of choosing [the choice of] at least one recombinant polynucleotide sequence formed at step (c) [to perform] and

using the chosen sequence as a source of fragments or as an assembly matrix during at least one repetition of steps (a), (b), (c), [(d), and (e)] or (d).

11. [Process according to one of claims 2 to 10, wherein it comprises the separation of] The method of claim 3, further comprising, before step (d), separating recombinant polynucleotide sequences formed at step (c) from the assembly matrix [(matrices) before step (e)].

12. [Process according to any one of claims 2 to 11, wherein it comprises the amplification of] The method of claim 3, further comprising, before step (d), amplifying recombinant polynucleotide sequences formed at step (c) [before step (e)].

13. [Process according to any one of claims 2 to 12, wherein it comprises] The method of claim 3, further comprising before step [(e)] (d), [the] cloning [of] the recombinant polynucleotide sequences formed at step (c) [, optionally after separation of recombinant strands from the matrix (matrices)].

14. [Process according to any one of claims 2 to 13,] The method of claim 1, wherein the ends of the fragments [produced] provided at step (a) are such that the fragments hybridize adjacently to one another on the assembly matrix [there can be hybridization adjacent to these ends on at least one assembly matrix at step (c) and ligation of these fragments with one another at step (d)].

15. [Process according to any one of claims 2 to 14,] The method of claim 14, wherein steps (b) and (c) [and (d)] are performed simultaneously.

16. [Process according to any one of claims 2 to 15,] The method of claim 14, wherein step (a) [consists in] comprises subjecting the polynucleotide sequences of the initial bank to hydrolysis by the action of one or several restriction enzymes.

17. [Process according to any one of claims 2 to 15, wherein the] The method of claim 14, wherein step (a) further comprises randomly fragmenting polynucleotide sequences from the bank of polynucleotide sequences [random fragmentation of polynucleotide sequences at step (a) is performed by any known enzymatic or mechanical method].

18. [Process according to any one of claims 2 to 13 and 15 to 17,] The method of claim 1, further comprising adding an enzyme at step (b) or (c) that specifically recognizes and degrades [enzymes able to recognize and degrade and/or cut in a specific manner the] any nonhybridized ends of the fragments when said nonhybridized ends cover other hybridized fragments on the same matrix [are added at step (c) and/or at step (d)].

19. [Process according to] The method of claim 18, wherein the enzyme is Flap endonuclease [is added at step (c) and/or at step (d)].

20. [Process according to any one of claims 2 to 15,] The method of claim 18, wherein [at least one specific,] the enzyme is a single-stranded exonuclease [able to recognize and degrade in a specific manner the nonhybridized ends of fragments when said ends cover other hybridized fragments on the same matrix is added at step (c) and/or (d)].

21. [Process according to any one of the preceding claims,] The method of claim 1, wherein a [preferably] thermostable ligase that is active at high temperature is used at step [(d)] (c).

22. [Process according to claims 18 and 19, wherein the endonucleases able to recognize and degrade and/or cut in a specific manner the nonhybridized ends of fragments added at step (c) and/or at step (d) have the same characteristics of thermoresistance and high-temperature activity as the ligase used at step (d)] The method of claim 18 or 19, further comprising using a thermostable ligase at step (c), wherein the enzyme that recognizes and degrades the nonhybridized ends is as thermostable as the thermostable ligase .

23. [Process according to claim 20, wherein the exonucleases able to recognize and degrade in a specific manner the nonhybridized ends of fragments added at step (c) and/or at step (d) have the same characteristics of thermoresistance and high-temperature activity as the ligase used at step (d).] The method of claim 20, further comprising using a thermostable ligase at step (c), wherein the enzyme that recognizes and degrades the nonhybridized ends is as thermostable as the thermostable ligase .

24. [Process according to any one of the preceding claims,] The method of claim 1, wherein the initial bank of polynucleotide sequences is produced from a wild gene by successive steps of controlled mutagenesis, by error prone PCR, by random chemical mutagenesis, by *in vivo* random mutagenesis, or by combining genes of near or distinct families within the same species or from different species so as to make available a variety of polynucleotide sequences in the initial bank.

25. [Process according to any one of claims 2 to 23,] The method of claim 1, wherein the initial bank of polynucleotide sequences consists of synthetic sequences [that will be fragmented at step (a) or that can constitute the fragments of step (a)].

26. [Process according to any one of claims 2 to 16 and 18 to 25,] The method of claim 1, wherein step (a) [consists in] comprises subjecting the initial bank to hydrolysis by the action of several different restriction enzymes or by the action of restriction enzymes having a large number of cutting sites on the polynucleotide sequences of the initial bank [, or in combining several restriction enzymes] .

27. [Process according to any one of claims 2 to 15 and 17 to 25,] The method of claim 17, wherein randomly fragmenting polynucleotide sequences from the bank of polynucleotide sequences comprises treating the polynucleotide sequences [step (a) consists of a random treatment] with DNAase I [from an initial bank of polynucleotide sequences].

28. [Process according to any one of claims 2 to 15 and 17 to 27,] The method of claim 17, wherein a fragment [fragments] produced by [a random treatment] the random fragmenting is [are] used as the assembly matrix at step (b) [matrices for one another, for hybridization during step (c) or during the reaction of steps (c) and (d) simultaneously].

29. [Process according to claims 2 to 16 and 18 to 26,] The method of claim 26, wherein a fragment [fragments] obtained at step (a) by a treatment with restriction enzymes is [are] used as the assembly matrix at step (b) [matrices for one another, for hybridization during step (c) or during the reaction of steps (c) and (d) simultaneously].

30. [Process according to claims 2 to 15 and 18 to 26,] The method of claim 1, wherein the fragments of step (a) are obtained by amplification reactions performed on polynucleotide sequences of the initial bank using initiated oligonucleotides, making it possible to produce fragments having sequences in common, said fragments acting as an assembly matrix for one another at step (b) or at step (c).

31. [Process according to any one of the preceding claims,] The method of claim 2, wherein the polynucleotide sequences of the initial bank [is] are fragmented into three or more fragments [n fragments at step (a), n being greater than or equal to 3].

32. [Process according to any one of the preceding claims,] The method of claim 1, wherein , in addition to the fragments and assembly matrix, [besides the matrix,] oligonucleotides of varying length, single- or double-stranded, are added at step (a) or (b) [or (c)] .

33. [Process according to any one of the preceding claims,] The method of claim 3, wherein, before step (d) [(e)], the recombinant polynucleotide sequences formed at step (c) are separated from the assembly matrix thanks to a marker present on the assembly matrix or on the recombinant polynucleotide sequences.

34. [Process according to any one of the preceding claims,] The method of claim 3, wherein the recombinant polynucleotide sequences formed at step (c) [obtained at step (d) and optionally cloned] are used [by any appropriate means] to select the recombinant polynucleotide sequences , formed during subsequent repetitions of step (c), [or the clones offering] that have advantageous characteristics compared with corresponding characteristics of reference sequences.

35. [Process according to] The method of claim 34, wherein the screening is performed by *in vitro* expression of recombinant polynucleotide sequences.

36. [Process according to any one of the preceding claims,] The method of claim 1, wherein the initial bank of polynucleotide sequences [consists of] comprises one or several restricted banks prepared by a prior performance of the method of claim 1 [process according to any one of claims 1 to 35, optionally mixed with other polynucleotide sequences] .